

**- Virus**

## Severity lessened as lungs get spared

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Aspate of new studies on lab animals and human tissues are providing the first indication of why the Omicron variant causes milder disease than previous versions of the coronavirus. In studies on mice and hamsters, Omicron produced less damaging infections, often limited largely to the upper airway: the nose, throat and windpipe. The variant did much less harm to the lungs, where previous variants would often cause scarring and serious breathing difficulty.

“It’s fair to say that the idea of a disease that manifests itself primarily in the upper respiratory system is emerging,” said Roland Eils, a computational biologist at the Berlin Institute of Health, who has studied how coronaviruses infect the airway. In November, when the first report on the Omicron variant came out of South Africa, scientists could only guess at how it might behave differently from earlier forms of the virus. All they knew was that it had a distinctive and alarming combination of more than 50 genetic mutations.

Previous research had shown that some of these mutations enabled coronaviruses to grab onto cells more tightly. Others allowed the virus to evade antibodies, which serve as an early line of defense against infection. But how the new variant might behave inside of the body was a mystery. “You can’t predict the behavior of virus from just the mutations,” said Ravindra Gupta, a virologist at the University of Cambridge.

Over the past month, more than a dozen research groups, including Dr. Gupta’s, have been observing the new pathogen in the lab, infecting cells in Petri dishes with Omicron and spraying the virus into the noses of animals. As they worked, Omicron surged across the planet, readily infecting even people who were vaccinated or had recovered from infections. But as cases skyrocketed, hospitalizations increased only modestly. Early studies of patients suggested that Omicron was less likely to cause severe illness than other variants, especially in vaccinated people. Still, those findings came with a lot of caveats.

For one thing, the bulk of early Omicron infections were in young people, who are less likely to get seriously ill with all versions of the virus. And many of those early cases were happening in people with some immunity from previous infections or vaccines. It was unclear whether Omicron would also prove less severe in an unvaccinated older person, for example. Experiments on animals can help clear up these ambiguities, because scientists can test Omicron on identical animals living in identical conditions. More than half a dozen experiments made public in recent days all pointed to the same conclusion: Omicron is milder than Delta and other earlier versions of the virus. On Wednesday, a large consortium of Japanese and American scientists released a report on hamsters and mice that had been infected with either Omicron or one of several earlier variants. Those infected with Omicron had less lung damage, lost less weight and were less likely to die, the study found.

Although the animals infected with Omicron on average experienced much milder symptoms, the scientists were particularly struck by the results in Syrian hamsters, a species known to get severely ill with all previous versions of the virus. “This was surprising, since every other variant has robustly infected these hamsters,” said Dr. Michael Diamond, a virologist at Washington University and a co-author of the study.

The reason that Omicron is milder may be a matter of anatomy. Dr. Diamond and his colleagues found that the level of Omicron in the noses of the hamsters was the same as in animals infected with an earlier form of the coronavirus. But Omicron levels in the lungs were one-tenth or less of the level of other variants.